

REMARKSStatus of the Subject Application and the Present Response

Claims 1-3, 5-13 and 15-44 are pending in the patent application, with claims 21-44 being withdrawn as directed to non-elected inventions. Claims 1-3, 5-13 and 15-20 are under examination and remain rejected in the instant office action.

With entry of the present response, Claims 1 and 11 are amended to specify that the recited chemical probe contains an alkene organic group. Support for the amendment is provided in the specification, e.g., at page 23, lines 2-4. In addition, claims 3 and 13 are amended to replace the recitation of "Amplex™ Red" with the chemical name of the compound denoted by the trademark. Support for the amendment is provided in the specification, e.g., at page 30, lines 20-25. Evidently, these amendments do not introduce any new matter.

Unless otherwise indicated, the amendments have been made to improve clarity or to expedite prosecution of the subject application, and should not be construed as acquiescence of any ground of rejections. Applicants present the following remarks and arguments to address the issues raised by the Examiner in the office action.

Objection to the specification

Objection to the specification is maintained on the ground that singlet oxygen belongs to the broader genus of reactive oxygen species, and that the reference in the specification to conversion of "singlet oxygen" into "reactive oxygen species" is therefore repugnant to the art-recognized definition of reactive oxygen species. Applicants reiterate their willingness to address this objection once an allowable subject matter in the subject patent application is indicated by the Examiner.

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Indefiniteness rejections under 35 U.S.C. § 112, 2<sup>nd</sup> Paragraph

The pending claims were rejected as allegedly indefinite due to the recitations of "specific" and "Amplex Red". Applicants do not agree with the rationale underlying these rejections. Nevertheless, in an effort to facilitate prosecution of the subject application, Applicants have herein amended the claims by deleting the term "specific" and also replacing the term "Amplex Red" with the chemical name of the active reagent denoted by the trademark, 10-acetyl-3,7-dihydroxyphenoxazine.

New matter rejection under 35 U.S.C. § 112, 1<sup>st</sup> paragraph

Claims 1-3, 5-13 and 15-20 remain rejected as allegedly failing to comply with the written description requirement. The Examiner asserts that the there is no support for the recitation in claims 1 and 11 of detecting probes that are oxidized in vivo by in vivo antibody-generated reactive oxygen species. The Examiner additionally alleges that "Amplex Red" recited in claims 3 and 13, and "specific" recited in claims 1 and 11 also constitute new matter. These rejections are respectfully traversed for the reasons on record and the additional clarifications provided below.

As an initial matter, Applicants note that the Examiner appears to have applied a verbatim and literal support standard in making the instant rejection. However, such is not the legal test for written description requirement. Rather, the written description requirement "does not require in haec verba antecedence in the specification." *Staehelin v. Secher*, 24 USPQ2d 1111, 1117 (Fed. Cir. 1991; emphasis added). All that is required is that "the description convey with reasonable clarity to person of skill in the art that the inventor was in possession of whatever is now claimed." *Vas-Cath v. Mazurka*, 935 F.2d

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1555, 19 USPQ2d 1111,1117 (Fed. Cir. 1991). If a person of ordinary skill in the art would have understood the inventor to have been in possession of the claimed invention at the time of filing, even if every nuance of the claims is not explicitly described in the specification, then the adequate written description requirement is met. *In re Alton*, 76 F.3d 1168, 1175, 37 USPQ2d 1578, 1584 (Fed. Cir. 1996; emphasis added).

Consistent with the case law, the MPEP also states that "[t]he subject matter of the claim need not be described literally (i.e., using the same terms or in haec verba) in order for the disclosure to satisfy the description requirement." (MPEP § 2163.02; emphasis added). Further, it should be emphasized that mere rephrasing of a passage does not constitute new matter. "A rewording of a passage where the same meaning remains intact is permissible." See *In re Anderson*, 471 F.2d 1237 (CCPA 1973) and MPEP 2163.07-I. Further, as stated in the MPEP, other than express disclosure, claim limitations can also be supported in the specification by implicit or inherent disclosure (See, e.g., MPEP. § 2163-I-B).

Applying the legal test to the instant case, Applicants cannot agree with the reasoning advanced by the Examiner in rendering and maintaining the present rejections. First, the Examiner asserts that Applicant's statement that "the claims do not expressly recite probes that are oxidized by in vivo antibody-generated reactive oxygen species" is contradicting Applicants' other remarks. Applicants wish to clarify that, contrary to the Examiner's apparent assumption, Applicants do not dispute that the claimed methods entail the detection of in vivo antibody-generated reactive oxygen species. Rather, what Applicants emphasized in the previous response was that the pending claims do not recite the term "in vivo." Applicants

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pointed this out because the new matter rejection previously raised by the Examiner appears to be directed to the alleged recitation of this term in the claims. Since the claims do not recite the term "in vivo," there is no basis for the alleged new matter.

In addition, the specification disclosed methods of detecting immunological responses or inflammatory responses by (a) administering a suitable chemical probe for a reactive oxygen species; (b) obtaining a sample from the mammal; and (c) analyzing the sample for oxidization products of the chemical probe (see, e.g., page 4, lines 13-17; and page 19, line 27 to page 20, line 3). The specification also disclosed that antibody-generated reactive oxygen species is indicative of immune responses or inflammatory responses (which are in vivo responses by nature) (see, e.g., page 4, line 17 to page 5, line 4; and page 21, lines 4-12). These disclosures undoubtedly provide support for the presently claimed invention. Applicants fail to see any new matter that is present in the pending claims but is not supported by such disclosures.

It is possible that the Examiner is concerned with the clause "wherein detection of the oxidized probe indicates the presence of the reactive oxygen species, thereby detecting an immunological response in the mammal." If such is the case, Applicants respectfully note that this clause certainly does not constitute new matter. This is because this clause does not represent an additional step or material not present in the original claims. Rather, it is merely intended to correlate the recited steps of the process claim with the preamble of the claim. Such a correlation is expressly taught throughout the specification, e.g., antibody can convert singlet oxygen to other reactive oxygen species, immune responses or inflammatory

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responses are associated with the presence of antibodies, and antibody-generated reactive oxygen species can oxidize an administered probe (see, e.g., page 18, lines 14-18; page 19, line 23 to page 7; and page 26, lines 21-23). Therefore, this clause has clear support in the specification, albeit not in a verbatim or literal manner. It at most represents a rephrasing or rewording of what was unequivocally disclosed in the specification, which should by no means be considered new matter. As clarified above, asserting that such a clause constitutes new matter is both factually incorrect and legally improper.

Regarding support for reciting the term "specific" in the previously introduced amendments, the issue of alleged new matter concerning this term is moot due to the presently introduced claim amendments. Nonetheless, for completeness of the records, Applicants note that the Examiner has mis-quoted disclosure in the specification as indicated by Applicants in Applicants' previous response. Specifically, Applicants pointed to page 24, lines 1-8 (not page 30, lines 15-18 as quoted by the Examiner) of the specification as support for the noted amendment. Using ozone as an example, the specification disclosed therein that ozone can be "detected and distinguished from other reactive oxygen species" by the use of indigo carmine. This is because oxidation of indigo carmine by ozone will yield an oxidized product, which will indicate that the oxidant is ozone, not another reactive oxygen species. Additional support for the recitation of a specific support is found in the specification, e.g., at page 23, lines 1-7. There, it was disclosed that the employed chemical probes contain an alkene that can be oxidized to generate a detectable oxidation product. These disclosures at least provide inherent and implicit, if not literal and explicit, support for the term "specific probe." As noted above,

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claim limitations can be properly supported by implicit or inherent disclosures in a patent specification.

The instant Office Action appears to also fault the recitation of "Amplex Red" as containing new matter. Again, this rejection is moot as a result of the present amendment. Nevertheless, Applicants do not understand the Examiner's rationale for the rejection as it was only stated in the office action that "Amplex Red was not administered to anything." In any event, Applicants direct the Examiner's attention to the disclosure in the specification, e.g., at page 30, lines 13-18. There, it was clearly stated that Amplex Red is a "chemical probe that reacts with reactive oxygen species . . ."

In view of the above clarifications, it is submitted that the presently claimed invention does not contain new matter. Withdrawal of the instant rejection is accordingly respectfully requested.

Enablement rejections under 35 U.S.C. § 112, 1<sup>st</sup> Paragraph

The Examiner maintained the rejection of the pending claims as allegedly not enabled. In maintaining the instant rejection, the Examiner repeats the assertions that the specification only discloses in vitro detection of oxidized products of a probe for a reactive oxygen species, that the specification provides no working examples evidencing the disclosed probes being oxidized in vivo by antibody-generated oxygen, and that the prior art showed that antibody generated reactive oxygen species do not have the redox potential in vivo to produce detectable oxidized probes. This rejection is again respectfully traversed for the reasons on records and the further remarks presented herein.

Applicants wish to remind the Examiner that, contrary to the assertions advanced by the Examiner in making and rendering the

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instant rejection, the present claims do NOT recite detecting *in vivo* an oxidized product of the administered probe. Rather, as clearly specified in the claims, upon administering the chemical probe (and allowing the oxidation reaction to occur), a sample is taken from the mammal, followed by detecting an oxidized product of the probe from the sample. Thus, it is clear that while the antibody-catalyzed production of reactive oxygen species occurs *in vivo*, the detection of the oxidized product of the administered probe actually occurs *in vitro*.

All the steps entailed by the claimed methods can be readily carried out in accordance with the subject disclosure and techniques well known in the art. There is certainly no question that the skilled artisans can readily administer a chemical probe disclosed in the specification to a mammal, obtain a sample thereafter from the mammal, and then perform an *in vitro* assay with the sample to detect an oxidized product of the administered probe.

Applicants have previously clarified that the prior art cited by the Examiner does not support the Examiner's assertions that the claimed methods are not enabled. In the present response, the Examiner requests that Applicants provide an affidavit or declaration in order for Applicants' clarifications to be of probative value. Applicants cannot agree with the Examiner's position. Accordingly to 37 CFR 1.132, an oath or declaration would be required to present "any evidence submitted to traverse the rejection or objection on a basis not otherwise provided . . ." (emphasis added). This clearly does not apply to the present case. This is because Applicants have clearly explained in the previous response that the Examiner's interpretation and application of the cited art to the present invention is scientifically incorrect. In other words,

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Applicants have already submitted evidence based on knowledge well known in the art to traverse the rejection. It is the Examiner's burden to consider Applicants' rebuttal and, if applicable, explain why Applicant's rebuttal is not persuasive. It will be entirely improper for the Examiner to simply disregard Applicants' reasoning and arguments, and instead require Applicants to provide an affidavit to further support Applicants' already submitted rebuttal.

In view of the foregoing, Applicants respectfully request that the rejection be withdrawn.

Rejection under 35 U.S.C. § 102

Claims 1, 2, 5, 7-12, 15 and 17-20 remain rejected as allegedly anticipated by Hewitt et al. For the reasons set forth in Applicants' previous response, Applicants do not consent to the appropriateness of the rejection. Nevertheless, in the interest of expediting prosecution, Applicants have herein further amended the pending claims which now specify that the administered chemical probe contain an alkene group. Evidently, an polypeptide or protein such as an IgG does not contain an organic alkene group. Therefore, even assuming for the sake of discussion that the IgG molecule administered to rats in Hewitt et al. can be considered a chemical probe, this reference still does not anticipate the presently claimed invention. The instant rejection should therefore be withdrawn.

CONCLUSION

In view of the foregoing, Applicant believes all claims now pending in this Application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

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If a telephone conference would expedite prosecution of this application, please telephone the undersigned attorney at 858-784-2937. If there are any additional fees (or overpayments) associated with this Response, or any Response associated with this application, the Director is hereby authorized to charge (or credit) our Deposit Account No. 19-0962.

Respectfully submitted,

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Date



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